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EXAMINER

GIBBS, TERRA C

ART UNIT

PAPER NUMBER

1635

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Please find below and/or attached an Office communication concerning this application or proceeding.

## Office Action Summary

Application No.

10/005,337

Applicant(s)

BENOIT ET AL.

Examiner

Terra C. Gibbs

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 28 February 2005.  
2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.  
3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 4,5,7,9,11,14,15,17,19,21,23,25,27,29,31,33-37 and 39-46 is/are pending in the application.  
4a) Of the above claim(s) 34-37 and 40-56 is/are withdrawn from consideration.  
5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.  
6) ☒ Claim(s) 4,5,7,9,11,14,15,17,19,21,23,25,27,29,31,33 and 39 is/are rejected.  
7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.  
8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.  
10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).  
11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
a) ☐ All b) ☐ Some \* c) ☐ None of:  
1. ☐ Certified copies of the priority documents have been received.  
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.  
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).  
\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)  
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)  
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)  
Paper No(s)/Mail Date \_\_\_\_\_.  
4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date \_\_\_\_\_.  
5) ☐ Notice of Informal Patent Application (PTO-152)  
6) ☐ Other: \_\_\_\_\_.

## DETAILED ACTION

### ***Continued Examination Under 37 CFR 1.114***

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on February 28, 2005 has been entered.

Claim 4 has been amended. New claims 40-56 are acknowledged.

Claims 4, 5, 7, 9, 11, 14, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33-37, and 39-56 are pending in the instant application. Claims 34-37 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made with traverse in the reply filed on October 20, 2003.

Newly submitted claims 40-56 are directed to an invention that is independent or distinct from the invention originally claimed for the following reasons: In response to the Restriction Requirement mailed September 23, 2003, Applicants elected, **with traverse**, Group I, drawn to a polynucleotide comprising a fragment of SEQ ID NO:1 or a fragment of a sequence that hybridizes under high stringency conditions with SEQ ID NO:1, wherein said polynucleotide specifically induces expression in cardiac cells *in vivo* of a gene which is operably linked to said polynucleotide. Applicant's traversal was

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found persuasive by the Examiner and Group II, drawn to a polynucleotide comprising a fragment of SEQ ID NO:2 or a fragment having at least 80% sequence identity to a fragment of SEQ ID NO:2, wherein said polynucleotide specifically induces expression in cardiac cells *in vivo* of a gene which is operably linked to said polynucleotide was also examined.

New claims 40-56 are drawn to a polynucleotide comprising SEQ ID NO:1 or a sequence having at least 93% identity to SEQ ID NO:1, wherein said polynucleotide in the absence of inverted terminal repeat sequences from human adeno-associated virus specifically induces expression in cardiac cells *in vivo* of a gene which is operably linked to said polynucleotide.

Applicants have received an action on the merits for the originally presented invention drawn to polynucleotides comprising **fragments** of SEQ ID NOs: 1 and 2, fragments of a sequence that hybridizes under high stringency conditions with SEQ ID NO:1, or a fragment having at least 80% sequence identity to a fragment of SEQ ID NO:2. New claims drawn to a polynucleotide comprising SEQ ID NO:1 or a sequence having at least 93% identity to SEQ ID NO:1 are directed to a non-elected invention. In fact, in Applicants response filed June 30, 2004, Applicants define a fragment as "an incomplete or isolated portion" as defined by The American Heritage College Dictionary (see Applicants response filed June 30, 2004, at page 11, first paragraph). In this regard, a polynucleotide comprising a **fragment** of SEQ ID NO:1 is distinct from a polynucleotide comprising SEQ ID NO:1 or a sequence having at least 93% identity to

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SEQ ID NO:1 because the latter is not an incomplete or isolated portion (fragment) of SEQ ID NO:1.

Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claims 40-56 are withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

Claims 4, 5, 7, 9, 11, 14, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, and 39 have been examined on the merits.

### ***Response to Arguments***

Applicants Amendment and Response filed February 28, 2005 has been considered. Rejections and/or objections not reiterated from the previous office action mailed June 30, 2004 are hereby withdrawn. The following rejections and/or objections are either newly applied or are reiterated and are the only rejections and/or objections presently applied to the instant application.

### ***Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 4, 5, 7, 9, 11, 14, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, and 39 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

Applicant is referred to the interim guidelines on written description published on December 21, 1999 in the Federal Register at Volume 64, Number 244, pp. 71427-71440.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed." (see page 1117). The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invention what is claimed." (See Vas-Cath at page 1116).

The specification provides adequate written description for a polynucleotide comprising SEQ ID NO:1, wherein said polynucleotide in the absence of inverted terminal repeat sequences from human adeno-associated virus specifically induces expression in cardiac cells *in vivo* of a gene which is operably linked to said polynucleotide (see Example 10). However, the claims are so broad to include a polynucleotide comprising a **fragment** of SEQ ID NO:2 or a **fragment** having at least 90% sequence identity to a fragment of SEQ ID NO:2, wherein said polynucleotide in

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the absence of inverted terminal repeat sequences from human adeno-associated virus specifically induces expression in cardiac cells *in vivo* of a gene which is operably linked to said polynucleotide. The specification as filed fails to adequately describe those polynucleotides comprising a fragment of SEQ ID NO:2 or those fragments having at least 90% identity to a fragment of SEQ ID NO:2 which retain the function of specifically inducing expression in cardiac cells *in vivo* of a gene which is operably linked to said polynucleotide as instantly claimed. This functional limitation itself is not sufficient to provide a structure/function relationship for meeting the written description requirement because it is not clear what structure the polynucleotides comprising a fragment of SEQ ID NO:2 or fragments having at least 90% identity to a fragment of SEQ ID NO:2 would have by the recitation of the functionality alone, "specifically induces expression in cardiac cells *in vivo* of a gene which is operably linked to said polynucleotide". The specification provides no guidance in this regard. The claimed invention as a whole is not adequately described if the claims require essential or critical elements which are not adequately described in the specification. Possession may be shown by actual reduction to practice, clear depiction of the invention in a detailed drawing, or by describing the invention with sufficient relevant identifying characteristics such that a person skilled in the art would recognize that the inventor had possession of the claimed invention. *Pfaff vs. Electronics, Inc.*, 48 USPQ2d, 1641, 1646 (1998).

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481, 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification

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provided only the bovine sequence.

Therefore, only a polynucleotide comprising SEQ ID NO:1, wherein said polynucleotide in the absence of inverted terminal repeat sequences from human adeno-associated virus specifically induces expression in cardiac cells *in vivo* of a gene which is operably linked to said polynucleotide meets the written description provision of 35 U.S.C. 112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. 112 is severable from its enablement provision (see page 1115).

### ***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 4, 5, 21, 23, 27, 31, 33, and 39 are rejected under 35 U.S.C. 102(b) as being anticipated by Kuo et al. (Development, 1999 Vol. 126:4223-4234).

### ***Response to Arguments***

It is noted that the same rejection was maintained in the last Office Action mailed June 30, 2004. In response to this rejection, Applicants argue that in order to anticipate



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a claim, a reference must teach every element of the claim. Applicants rely on MPEP § 2131. Applicants argue that none of the constructs tested by Kuo et al. have the properties recited by claim 4 drawn to a fragment of SEQ ID NO:2 or a fragment having at least 90% sequence identity to a fragment of SEQ ID NO:2, wherein said polynucleotide in the absence of inverted terminal repeat sequences from human adeno-associated virus specifically induces expression in cardiac cells *in vivo* of a gene which is operably linked to said polynucleotide. Applicants contend that Kuo et al. tested the transcriptional activity of certain sequences upstream of the *mouse*, not the *human* CARP gene.

Applicants contention has been considered but is not found persuasive by the Examiner because while Kuo et al. tested the transcriptional activity of certain sequences upstream of the mouse, not the human CARP gene, the instant claims are broadly drawn to a polynucleotide comprising a **fragment** of SEQ ID NO:2 or **fragments** having at least 90% sequence identity to a fragment of SEQ ID NO:2. As discussed below, Kuo et al. clearly teach fragments having at least 90% sequence identity to a fragment of SEQ ID NO:2, wherein said polynucleotide in the absence of inverted terminal repeat sequences from human adeno-associated virus specifically induces expression in cardiac cells *in vivo* of a gene which is operably linked to said polynucleotide as instantly claimed.

Applicants independently argue three specific constructs disclosed by Kuo et al., namely the 213 bp fragment of the mouse CARP promoter, between nucleotides -166 and +47, p0.176Luc (-176 to +47) and p0.295Luc (-295 to +47). Regarding the first

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construct, the 213 bp fragment of the mouse CARP promoter, between nucleotides -166 and +47, Applicants argue that this fragment shows activity only when present as a tandem repeat with nucleotides -166 to -39 of the mouse CARP gene. Applicants point the Examiner to Figure 3 (p2x0.128TATA Luc). Applicants contend that this tandem repeat cannot be characterized as either a fragment of SEQ ID NO:2 or a fragment with 90% identity to SEQ ID NO:2.

This argument has been fully considered but is not found persuasive because the Examiner is not arguing that the tandem repeat is a fragment of SEQ ID NO:2 or a fragment with 90% identity to SEQ ID NO:2. Instead, the Examiner is arguing that the 213 bp fragment of the mouse CARP promoter, between nucleotides -166 and +47 is a fragment having at least 90% sequence identity to a fragment of SEQ ID NO:2. This is best demonstrated in Applicant's Exhibit A which is a BLAST sequence comparison between the 213 bp fragment of the mouse CARP promoter, between nucleotides -166 and +47 and SEQ ID NO:2 of the instant invention. It is noted that Exhibit A demonstrates that the 213 bp fragment of the mouse CARP promoter, between nucleotides -166 and +47 shares 79% identity overall with a fragment of SEQ ID NO:2. However, Exhibit A is also replete with fragments having at least 90% sequence identity to a fragment of SEQ ID NO:2. In fact, many fragments exhibit 100% sequence identity to a fragment of SEQ ID NO:2. For example, compare Applicant's Exhibit A Query<sup>1</sup> sequence at nucleobases -147 to -134, -131 to -102, and -58 to -41 with Sbjct<sup>2</sup> nucleobases 1867 to 1880, 1883 to 2011, and 2056 to 2073, respectively. Further, the claims are drawn a polynucleotide comprising a fragment of SEQ ID NO:2 or a fragment

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having at least 90% sequence identity to a fragment of SEQ ID NO:2. The term "comprising" is open language and therefore the fragments having at least 90% sequence identity to a fragment of SEQ ID NO:2 as instantly claimed can additionally contain the tandem repeat as disclosed by Kuo et al. In this regard, the 213 bp fragment of the mouse CARP promoter, between nucleotides -166 and +47 clearly anticipate the claims. The Examiner would like to point out that Kuo et al. disclose regarding construct p2x0.128TATA lacZ, "transgene expression was detected only in the heart, not in the somites, and **cardiac expression** of the transgene was specific to cardiomyocytes in the conotruncal segment of the primitive heart" (see page 4227, first column, last sentence and Figures 4E, IJ and 5D). The Examiner would like to further point out that the instant specification at page 4, [009] recites, "a region of 213 bp of the promoter between nucleotides -166 and +47, relative to the transcription start position +1, was sufficient to confer cardiospecific expression". Therefore, contrary to Applicants contention, p2x0.128TATA lacZ clearly anticipates the instant claims.

Applicants argue that construct p0.176Luc (-176 to +47) exhibits no activity. This argument is found persuasive. The Examiner agrees that construct p0.176Luc (-176 to +47) only exhibits activity and cardiac expression in the presence of the tandem repeat as discussed above (see construct p2x0.128TATA lacZ).

Applicants also argue that construct p0.295luc (-295 to +47) has promoter activity and exhibits 83% sequence identity to a fragment of SEQ ID NO:2 (see Exhibit B). Applicants contend that this construct does not anticipate the invention since the claims have been amended to recite "90% sequence identity". Applicants also contend that

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Kuo et al. do not disclose that construct p0.295luc (-295 to +47) “specifically induces expression in cardiac cells *in vivo*” as recited by claim 4. Applicants point the Examiner to page 4227.

This argument and contention has not been found persuasive by the Examiner because construct p0.295luc (-295 to +47) is a fragment having at least 90% sequence identity to a fragment of SEQ ID NO:2. This is best demonstrated in Applicant’s Exhibit B which is a BLAST sequence comparison between construct p0.295luc (-295 to +47) and SEQ ID NO:2 of the instant invention. It is noted that Exhibit B demonstrates that the p0.295luc (-295 to +47) construct shares 83% identity overall with a fragment of SEQ ID NO:2. However, Exhibit B is also replete with fragments having at least 90% sequence identity to a fragment of SEQ ID NO:2. In fact, several fragments exhibit 100% sequence identity to a fragment of SEQ ID NO:2. For example, compare Applicant’s Exhibit B Query<sup>1</sup> sequence at nucleobases -207 to -184 and -137 to -102 with Sbjct<sup>2</sup> nucleobases 1803 to 1826 and 1882 to 1918, respectively. In this regard, construct p0.295luc (-295 to +47) clearly anticipate the claims. Referring to page 4227, the Examiner would like to point out that Kuo et al. disclose regarding construct p0.295luc (-295 to +47), “expression of the transgene was specific to both the myocardium of the heart and the somites, and cardiac expression was first detected at around E9.95. **Cardiac expression** of the transgene was restricted to the conotruncal and right ventricular segments of the primitive heart” (see page 4227, first column, last paragraph, and Figures 4D, H, and 5C). Therefore, contrary to Applicants contention, construct p0.295luc (-295 to +47) clearly induces expression in cardiac cells *in vivo* as

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recited in claim 4.

***Conclusion***


No claims are allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Terra C. Gibbs whose telephone number is 571-272-0758. The examiner can normally be reached on 9 am - 5 pm M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Wang Andrew can be reached on 571-272-0811. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

tcg  
May 26, 2005

  
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